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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/719,125	11/21/2003	Franz Birke	1/1421	2235

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EXAMINER	
HENLEY III, RAYMOND J	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 08/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/719,125	BIRKE ET AL.	
	Examiner	Art Unit	
	Raymond J. Henley III	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *9-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/1/04 & 11/1/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

CLAIMS 1-13 ARE PRESENTED FOR EXAMINATION

Applicants' Reply to Restriction Requirement filed April 27, 2006 and Information Disclosure Statements filed March 1, 2004 and November 1, 2004 have been received and entered into the application.

As reflected by the attached, completed copies of form PTO/SB/08(a/b), (4 sheets), the Examiner has considered the cited references.

Restriction/Election

In response to the restriction requirement set forth in the previous Office action dated February 16, 2006, Applicants have elected, with traverse, the invention of Group I, claims 1-8 and 13, directed to a pharmaceutical composition/kit containing a leukotriene B_4, (LTB_4), antagonist and a cyclooxygenase-2, (COX II) or a combined COX I/COX II inhibitor, as well a pharmaceutically acceptable carrier or diluent.

Applicants have traversed the requirement for restriction on the grounds that there would not be an undue burden placed on the Examiner in examining all inventions present in the claims as originally filed. Applicants indicate that such is the case because the two inventions, (i.e., the invention of Group II is directed to claims reciting methods of preventing or treating any one of a listing of 27 different disease states where the composition of Group I is administered, as shown in present claim 9), are sufficiently related that a search for one invention would uncover relevant art for the other.

Applicants' traverse has been given careful consideration, but fails to persuade the Examiner of error. In analyzing the claims of the elected invention against the prior art for

determining the patentability thereof, the Examiner is not constrained to any one particular disease state or condition. Thus, a proper search in the art would only need to be as detailed as the identities of the active agents for use in a therapeutic setting. In considering the claims which define a method of preventing or treating, however, a detailed analysis would be necessary for each of the twenty-seven disease states listed in present claim 9. Such analysis would not only have to take into consideration the identity of the active agents, but also the etiology, pathophysiological manifestations, known treatment modalities, and other aspects for each disease known to one of ordinary skill in the art at the time the present invention was made.

Thus, while both grouped inventions share the common element of a combination of two types of active agents, a search for each group would not be co-extensive and a search for both would require more items of consideration than is deemed reasonable for a single invention.

Accordingly, for the above reasons, as well as to ensure a proper, quality examination of the presently claimed subject matter, the Examiner maintains the requirement for restriction to be proper. Therefor, the requirement to restrict the claims, as set forth in the previous Office action is made **FINAL**.

Claims 9-12 are withdrawn from further consideration under 37 C.F.R. § 1.142(b). As set forth in the previous Office action, the non-elected claims are subject to being rejoined with the claims examined herein upon an indication of allowable subject matter, as well as the other conditions set forth at page 3, last two paragraphs, of the previous Office action.

Claims 1-8 and 13 are herein examined on the merits.

Claim Interpretation

In claim 3, the transitional phrase, "consisting essentially of" is interpreted in the same

manner as "comprising". Such is proper because the present specification fails to clearly indicate what the basic and novel characteristics of the claimed composition actually are. "For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of' will be construed as equivalent to "comprising." See, e.g., PPG, 156 F.3d at 1355, 48 USPQ2d at 1355", (see MPEP § 2111.03, fourth paragraph).

Claim Rejection - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-8 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Schromm et al., (U.S. Patent No. 6,197,824, cited by Applicants) or Anderskewitz et al., (U.S. Patent No. 5,731,332, cited by Applicants) in view of Gregory et al., (U.S. Patent No. 6,172,096, cited by Applicants).

Schromm et al. teach a pharmaceutical composition, suitable for topical, oral, transdermal, nasal, parenteral or inhaled administration, (col. 3, lines 20-22), which comprises, for oral administration, from 10 to 500 mg, for example, (col. 3, lines 30-31), of a LTB_4 antagonistic benzamidine compound corresponding to the presently claimed compound as represented in present claim 1, where (i) A is "A2" , (ii) the propyl group which is attached at the ortho position of the phenylene group in A2 corresponds to the patentees' R_1 group which may be an unbranched C_{1-6} alkyl and (ii) R may represent either a hydrogen or a group of the formula $-CO_2-R'$, in which R' represents a C_{1-6} alkyl, (note, in the reference, Applicants' latter R group is identified as "C_{1-6} alkoxycarbonyl", which is illustrated in compound 33 at cols. 21-22, for example), (see col. 1, the structure corresponding to general formula 1 as well as compounds 3, 9, 24, 28, 42, 45 and 59 at cols. 7-8, 9-10, 17-18, 19-20, 25-26, 27-28 and 33-34, respectively). The patentees further show that carbohydrate diluents may be employed in the preparation of the compositions, (see col. 3, line 50, "glucose" and line 63, "Lactose, powdered").

Anderskewitz et al. teach a pharmaceutical composition, suitable for topical, oral, transdermal, nasal, parenteral or inhaled administration, (col. 5, lines 24-26), which comprises, for oral administration, from 10 to 500 mg, for example, (col. 5, lines 33-34), of a LTB_4 antagonistic benzamidine compound corresponding to the presently claimed compound as represented in present claim 1, where A is "A1", (e.g., see col. 1, line 19 – col. 2, line 62), and in particular the compound depicted in present claim 3, (see cols. 15-16, third compound from the top). The patentees further show that carbohydrate diluents may be employed in the preparation of the compositions, (see col. 5, line 54, "glucose" and col. 6, line 2, "Lactose, powdered").

The differences between the above and the claimed subject matter lie in that neither Schromm et al. nor Anderskewitz et al. highlight (i) a combination of their respective LTB_4 antagonistic benzamidine compound with a cyclooxygenase, (COX) type-1 or type-2 inhibiting compound and (ii) the presently claimed ingredient amounts/proportioning and a kit.

However, the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains because of the further teachings in Schromm et al. and Anderskewitz et al., as well as the knowledge one of ordinary skill in the art would have had of other references, as explained below.

In particular, Schromm et al. and Anderskewitz et al. teach that their compounds are effective for treating such disorders as arthritis and asthma, (see the former at col. 3, line 3 and the latter at col. 5, line 7), and that their compounds may be used in conjunction with other substances, such as those which are used for the same indications, (see the former at col. 3, lines 16-18 and the latter at col. 5, lines 20-22), while one of ordinary skill in the art was aware that not only were COX-2 inhibitory compounds known for treating arthritis and or asthma, but they have been successfully combined with LTB_4 antagonists for these very same purposes. In support of this position, the Examiner relies on Gregory et al. who teach combinations of LTB_4 antagonists and COX-2 inhibitory compounds for the treatment of arthritis or asthmatic disorder, (col. 4, line 53 – col. 5, line 41). Gregory further teaches that the COX inhibitory compounds may possess both COX-1 and COX-II inhibitory activity and that those that inhibit COX-II to a greater extent than COX-1 are preferred, (col. 6, lines 38-49). Insofar as Gregory et al. do not

limit themselves to any specifically named COX inhibitors, it is thus believed that the selection of any such inhibitor from those known to one of ordinary skill in the art would have been a matter well within his/her purview. The artisan would have been motivated to make such a selection because Gregory indicates that COX inhibitors, which preferentially inhibit COX-II, would be useful in accomplishing their goals.

Further, respecting the amounts/ratios of active agents, it has been held that "Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955)" (see MPEP 2144.05(II)). One of ordinary skill in the art would have necessarily needed to determine the optimum amounts/ratios of active agents. In this respect, Gregory teaches that the pharmaceutical compositions may comprise from 0.1 to 2000 mg of active ingredients, (col. 29, lines 33-34). While this is not the claimed range of from 1 to 10,000 milligrams, the claimed range encompasses the range highlighted in Gregory et al. Further, Gregory does in no way limit his invention to only those amounts/ratios highlighted. It is believed that other amounts/ratios would have also been obvious because the determination of the optimum dosage regimen to employ with the presently claimed active agents would have been a matter well within the purview of one of ordinary skill in the art and such determination would have been made in accordance with a variety of factors. These would have included the age, weight, sex, diet and medical condition of the patient, severity of the disease, the route of administration, pharmacological considerations such as the

activity, efficacy, pharmacokinetics and toxicology profiles of the particular compound employed, whether a drug delivery system is utilized and whether the compound is administered a part of a drug combination. Thus, the dosage regimen that would have actually been employed would have varied widely and, in the absence of evidence to the contrary, the currently claimed specific dosage amounts/ratios are not seen to be inconsistent with those that would have been determined by the skilled artisan.

Also, while neither one of the patentees employs the term "kit", (compare to present claim 13), the teachings provided by the patentees provide for a composition that is just as detailed as the elements of present claim 13. Accordingly, it is not seen that the mere label of the composition as "a kit" imparts patentability to the claimed subject matter.

In summary, given the knowledge of the teachings of Schromm et al., Anderskewitz et al. and Gregory et al. it would have clearly made obvious to one of ordinary skill in the art the presently claimed subject matter. Further, given (i) the express teachings in Schromm et al. and Anderskewitz et al. to combine the LTB_4 antagonists with other compounds having the same utility and (ii) the showing in Gregory et al. that LTB_4 antagonists and COX inhibitory compounds have been combined for the treatment of the same conditions as in the primary references, such a person skilled in the art would have been motivated to do what Applicants are now claiming to do.

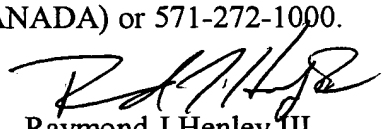
Accordingly, for the above reasons, the claims are deemed properly rejected.

None of the claims are currently in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Raymond J. Henley III whose telephone number is 571-272-0575. The examiner can normally be reached on M-F, 8:30 am to 4:00 pm Eastern Time.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Raymond J Henley III
Primary Examiner
Art Unit 1614

August 28, 2006